

**REMARKS**

The foregoing amendment amends claims 1, 12, 30, 32, 39, 40, 43, 46, 47 and 48, cancels claim 49 and adds new dependent claim 50. Pending in the application are claims 1-3, 5-24, 26-48 and 50, of which claims 1, 12, 30, 32, 39, 40, 43 and 46-48 are independent. The following comments address all stated grounds for rejection and place the presently pending claims, as identified above, in condition for allowance.

Independent claims 1, 12, 30, 32, 39, 40, 43, 46, 47 and 48 are amended to include the subject matter of canceled claim 49, which specifies that the meniscus of the virtual wall is substantially co-planar with the wall of the separation channel in which the meniscus is formed, as described on page 10, lines 6-7 of the original specification and as shown in Figures 4A and 4B. The recitation “co-planar” is intended to specify that the meniscus aligns with the side wall and is the same thickness as the wall, such that the meniscus, not the liquid in the channel or air surrounding the system, essentially replaces the removed portion of the side wall creating the fluid interface port. The top of the meniscus aligns with the top, outer end of the side wall, while the bottom aligns with the lower, inner end of the wall, and the meniscus fills the opening in the wall. Because the volume of the meniscus is measured based on the bottom edge of the meniscus, which aligns with the bottom edge of the opening at the inner side of the side wall, the dead volume of the fluid within the actual opening is significantly minimized, and preferably zero.

Independent claims 1, 12, 30, 32, 39, 40, 43, 46, 47 and 48 are also amended to remove the phrase “so as to minimize a total volume of the fluid interface port”. *No new matter is added.*

Amendment and/or cancellation of the claims is not to be construed as an acquiescence to any of the objections/rejections set forth in the instant Office Action, and was done solely to expedite prosecution of the application. Applicant reserves the right to pursue the claims as originally filed, or similar claims, in this or one or more subsequent patent applications.

**35 U.S.C. §112 Rejections**

In the Office Action, the Examiner rejects claims 1-3, 5-24 and 26-49 under 35 U.S.C. §112 as being indefinite. Applicants have amended independent claims 1, 12, 30, 32, 39, 40, 43,

46, 47 and 48 to address the Examiner's concern and request that the rejection under 35 U.S.C. §112 be reconsidered and withdrawn.

### **35 U.S.C. §103 Rejections**

In the Office Action, the Examiner rejects claims 1-3, 5-24 and 26-49 under 35 U.S.C. §103. Applicants traverse the rejection and submit that the pending claims distinguish patentably over the cited references.

#### **Obviousness Rejection over Heller in view of McCormick or Amigo**

The Examiner rejects claims 1, 2, 5-8, 30-37, 39-41, 43, 44 and 46-49 under 35 USC §103(a) as being unpatentable over Heller *et al.* in view of McCormick or Amigo. Applicants respectfully disagree and submit that the claims distinguish patentably over the cited references. To expedite allowance of the application, Applicants have amended the independent claims to include the subject matter of claim 49. The independent claims now specify that the meniscus of the virtual wall is substantially co-planar with the side wall of a channel in which the meniscus is formed and positioned.

As recognized by the Examiner, the Heller reference, which is directed to an electrophoretic separation device, does not disclose a fluid interface port having the claimed configuration. According to the Examiner, because the McCormick and Amigo references disclose microfluidic systems with covers for the channels having a thickness that is 10 microns, it would be obvious to modify the device of Heller to have a channel cover that is as thin as 10 microns. In modifying the depth of a channel cover in Heller to be 10 microns, the Examiner considers the limitation of a port diameter larger than the port depth to be met by the combination of references.

As also recognized by the Examiner, the Heller reference also does not disclose the claimed virtual wall and port dead volume of zero or less than a picoliter. The Examiner considers it obvious to use a shallow channel in the device of Heller, because no explicit channel depth is recited in Heller, which the Examiner considers to meet these recitations.

The Examiner also considers the Heller device to form a meniscus that is a virtual wall at the application area A of the electrophoretic separation device. The Examiner further indicates

that a meniscus anywhere from the upper to lower surface of an interface port can be described as “coplanar”, and that the subject matter of claim 49 is therefore also obvious.

Applicants maintain that the cited references, alone or in combination, do not teach or suggest a separation device including one or more fluid interface ports, each having a dead volume of less than about one *picoliter*, formed in the side wall of a separation channel having a virtual wall formed by a separation medium disposed in the interior of the separation channel, and which each virtual wall having a meniscus surface that is substantially co-planar with the side wall channel in which the virtual wall is formed, as recited in independent claims 1, 12, 30, 32, 39, 40, 43 and 46-48. In fact, Applicants submit that the cited references teach *away* from the claimed invention, and that motivation to combine the references to render the conclusion that the claims are obvious is lacking.

The recited fluid interface ports have a disk shape, with the virtual wall meniscus filling the boundary of the fluid interface port, as shown in Figure 4A, and described on page 9, line 20, to facilitate *direct* access to the channel interior. According to the Examiner, a meniscus that forms anywhere from the upper to lower surface of the interface port can be described as “co-planar” with the sidewall channel. However, as described above, the term “co-planar” requires that the meniscus substantially align with the side wall at the top and bottom and have substantially the same thickness as the side wall, not that the meniscus be formed “anywhere” from the upper to lower surface. The meniscus forming the virtual wall in the claimed invention *replaces* the removed portion of the side wall, and therefore is formed in the same plane as the side wall. The plane defining the meniscus is the same as the plane forming the wall, not a subset that overlaps a portion of the side wall, as assumed by the Examiner. Therefore, the cited references do not disclose the claimed fluid interface port forming a virtual wall having a meniscus that is co-planar with the side wall in which the meniscus is formed. Even if the Heller reference discloses a meniscus in the application areas A, the meniscus does not and cannot exist co-planar to a side wall having an opening in which the meniscus is formed. Rather, if the application areas A in Heller do indeed form a meniscus, the meniscus can only exist in a portion of the application area, not co-planar to a side wall, and does not form a virtual wall.

Furthermore, Applicants maintain that the Examiner has not pointed to an adequate and objective reason for combining the cited references in rendering the conclusion that claims 1-3,

5-24 and 26-48 are obvious, though even in combination, the Heller reference, the McCormick reference and/or the Amigo reference fail to disclose the claimed invention. Applicants maintain that motivation to combine and/or modify the references, which is required under 35 U.S.C. §103, is lacking. The “lack of explicit disclosure” cited by the Examiner in the Office Action does not amount to the requisite motivation to modify the teachings of Heller in view of the McCormick and/or Amigo reference. Because the Examiner has not provided a motivation, a *prima facie* case of obviousness has not been properly made. For example, according to the Examiner, motivation to reduce the thickness of the cover in Heller in view of the McCormick or Amigo references is the reduction of material consumption and manufacturing costs. However, the reduction of a cover thickness to such a precise and small amount would likely *increase* manufacturing costs, and likely make manufacture more difficult due to the scale, which teaches *away* from the combination.

In addition, there is no indication that reduction of the depth of the port in the device of Heller to match the depth described in McCormick or Amigo would result in a fluid interface port having a diameter greater than the depth, as set forth in the claims 1, 2, 5-8, 30-37, 39-41, 43, 44 and 46-48. There is no indication that a modification of the cover in the Heller device to a shallow depth would result in an application area A having a disk shape and capable of forming a virtual wall. Rather, it would appear that a reduction in the depth in Heller would require a similar reduction in the diameter of the application areas A. There is nothing in any of the cited references to suggest that the general shape of the application areas A in Heller could or should be modified.

In fact, the Heller reference teaches *away* from the claimed fluid interface port and the combination of references, because the Heller reference specifies, in column 5, lines 30-37, that the injection area A is preferably enlarged relative to the injection channel of the electrophoresis device, which teaches *away* from a fluid interface port capable of forming a virtual wall, in particular a fluid interface port with minimal dead volume. The modification of the Heller application areas A to have a disk shape, in particular a disk shape capable of forming a virtual wall when a fluid fills the channel, would require significant redesign and engineering. Because the Heller reference specifies that it is preferable to have a large injection area, it would be difficult to restructure the device of Heller to include the claimed fluid interface port.

In addition, Heller teaches that the cover for the channels may be a film, which precludes formation of a fluid interface port in a side wall defining a channel (see column 6, lines 1-2), as recited in the claims.

For at least the foregoing reasons, the cited Heller, McCormick and Amigo references fail to disclose or make obvious the claimed invention.

*Obviousness Rejection over Simpson in view of Howitz*

Regarding the rejection of claims 1-3, 5-8, 12-2, 26, 30-36 and 38-49 under 35 U.S.C. §103 as being unpatentable over the Simpson reference in view of the Howitz reference, Applicants maintain, as submitted in previous arguments, that the combination of the Simpson reference and the Howitz reference fails to anticipate the invention or render the claims obvious. As recognized by the Examiner, Simpson does not disclose the claimed fluid interface port having a meniscus forming a virtual wall. According to the Examiner, because the Howitz reference discloses a device having capillaries containing menisci at the top portion thereof, it would be obvious to modify the device of Simpson to include capillaries forming such menisci as fluid interface ports.

However, even in combination, the references fail to disclose the claimed invention. In particular, as shown in the figure of Howitz, the meniscus of Howitz is formed only in a top portion of the capillary and is not co-planar with the side wall in which the capillaries are formed, as required by the claims. It would be impossible for the meniscus to have the same thickness as and be co-planar with the side wall, because Howitz requires the capillaries to have an extended length. The capillaries create a large dead volume of liquid in each capillary below the meniscus, in contrast to the claimed invention.

As recognized by the Examiner, the combination of the Simpson and Howitz references fails to disclose the limitation that the port be wider than it is deep so as to form a disk shape. However, the Examiner considers that, because the Howitz reference discloses variation of the length of the capillary, the choice of a shorter length would be obvious. Applicants disagree and submit that the Howitz reference *requires* that the capillaries be shaped like capillaries, i.e., with an elongated channel shape, rather than disk-shape. Even if the capillaries were shortened,

which the Examiner considers to be an obvious modification, there is no teaching, suggestion or motivation to change the overall shape of the capillaries to have a diameter that is significantly larger than the depth. In addition, the Howitz reference would require significant redesign and reengineering to change the shape of the capillaries to the recited shape set forth in the present application. In fact, it is likely that the Howitz device could not properly operate at the shorter length or with a disc shaped fluid interface port.

Furthermore, the independent claims now require that the meniscus of the virtual wall be co-planar with the side wall in which a fluid interface port is formed. Even in combination, the cited Simpson reference and Howitz reference do not disclose this feature. As set forth in the present invention the term “co-planar with a side wall channel” does not encompass a meniscus that forms *anywhere* from the upper to lower surface of an interface port formed in the side wall. Rather, the co-planar meniscus aligns at the top and bottom with the side wall, with the meniscus, not fluid, essentially filling the opening in the side wall and replacing the removed side wall. As discussed, the cited references do not disclose this feature, because the Howitz reference merely discloses capillaries filled almost entirely with liquid, with a meniscus formed *only* at the top of the capillary, which is not co-planar with the side wall, but rather co-planar with only a small, upper portion of the side wall. Therefore, because Applicants require that a co-planar meniscus essentially replace and fill an opening, with the top and bottom of the co-planar meniscus aligning with the top and bottom of the side wall at the opening in the side wall, the cited references clearly do not anticipate the claimed invention.

Furthermore, as previously discussed, there is no motivation to modify the teachings of the Howitz reference and/or the Simpson reference, as required to make an obviousness rejection.

*Obviousness Rejection over Simpson in view of Howitz, and further in view of Bjornson et al. and/or Sundberg et al.*

Regarding the rejection of claims 9-11, 27-29, 37 as being unpatentable over Simpson *et al.* and Howitz as applied to claims 1 and 12 and further in view of Bjornson *et al.* and/or Sundberg *et al.* as described above, claims 1 and 12 distinguish patentably over the combination of the Simpson reference and the Howitz reference. Therefore, claims 9-11, 27-29 and 37 also distinguish patentably over the cited references.

Obviousness Rejection over Simpson in view of Heller and either McCormick et al. or Amigo

The Examiner also rejects claims 1-3, 5-8, 12-24, 26, 30-37 and 38-49 under 35 U.S.C. §103 as being unpatentable over Simpson et al. in view of Heller *et al.* and either McCormick *et al.* or Amigo. As described above, the cited references, alone or in combination, fail to disclose the claimed invention. Specifically, the cited references lack a teaching or suggestion of a fluid interface port in a microfluidic system that is disk-shaped (i.e., the diameter is substantially greater than the depth), has minimal dead volume and creates a meniscus out of fluid in a channel that is co-planar with a side wall of the channel in which the fluid interface port is formed, as set forth in independent claims 1, 12, 30, 32, 39, 40, 43, 46, 47 and 48.

Obviousness Rejection over Simpson in view of Heller and either McCormick et al. or Amigo, and in further view of Bjornson

Regarding the rejection of claims 9-11 and 27-29 as being unpatentable over Simpson, Heller, McCormick or Amigo and further in view of Bjornson, the independent claims from which these claims depend are patentable over the cited references. Therefore, these claims are also patentable.

As described above, all pending claims distinguish patentably over the cited references. For at least these reasons, Applicants request that the rejections under 35 U.S.C. §112 and 35 U.S.C. §103 be reconsidered and withdrawn.

**CONCLUSION**

For at least these reasons, Applicants respectfully submit that all pending examined claims are patentable, and request that the objections and rejections be reconsidered and withdrawn.

In view of the above amendment, applicant believes the pending application is in condition for allowance.

Dated: April 14, 2006

Respectfully submitted,

By David R. Burns  
David R. Burns

Registration No.: 46,590  
LAHIVE & COCKFIELD, LLP  
28 State Street  
Boston, Massachusetts 02109  
(617) 227-7400  
(617) 742-4214 (Fax)  
Attorney/Agent For Applicant